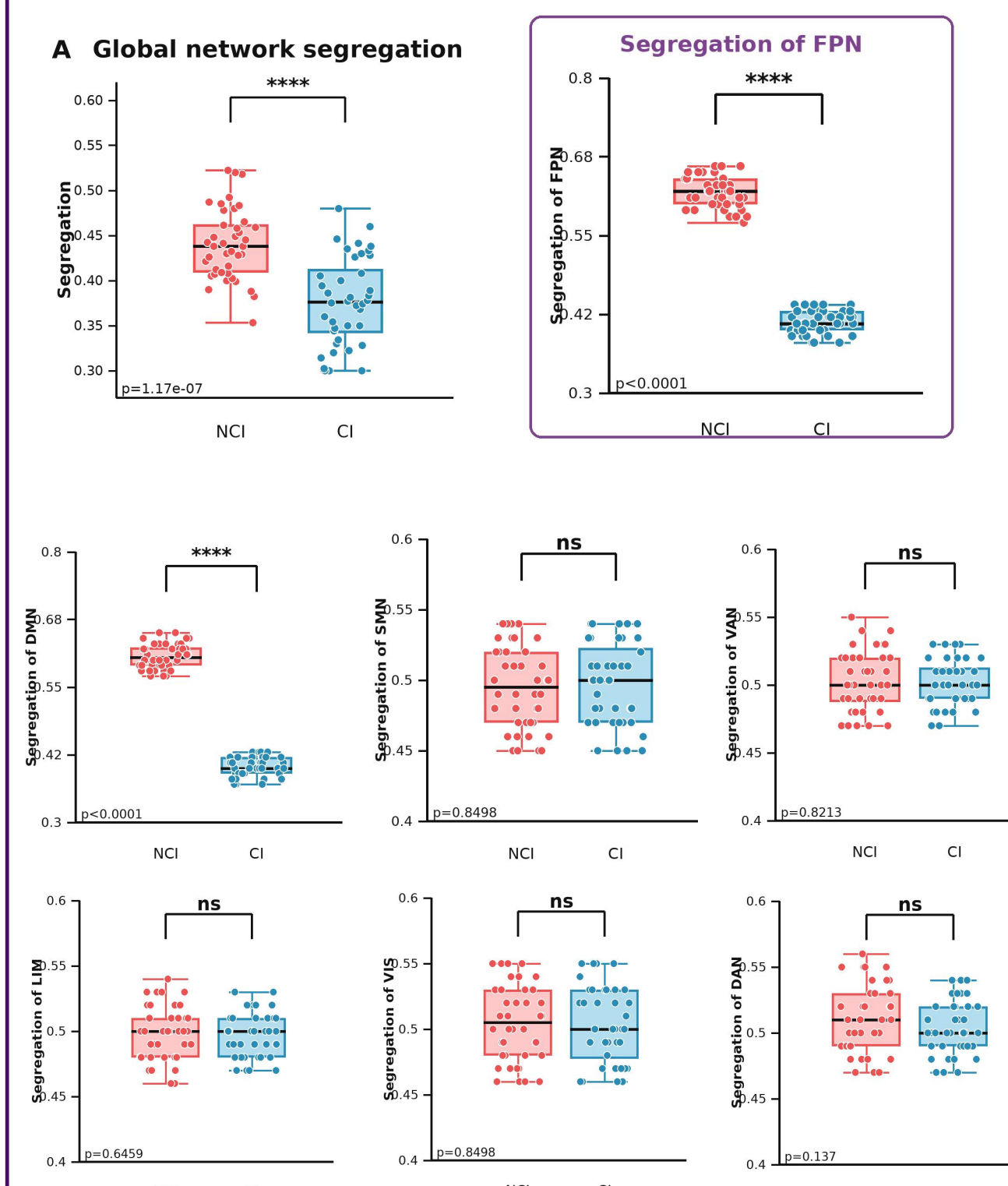
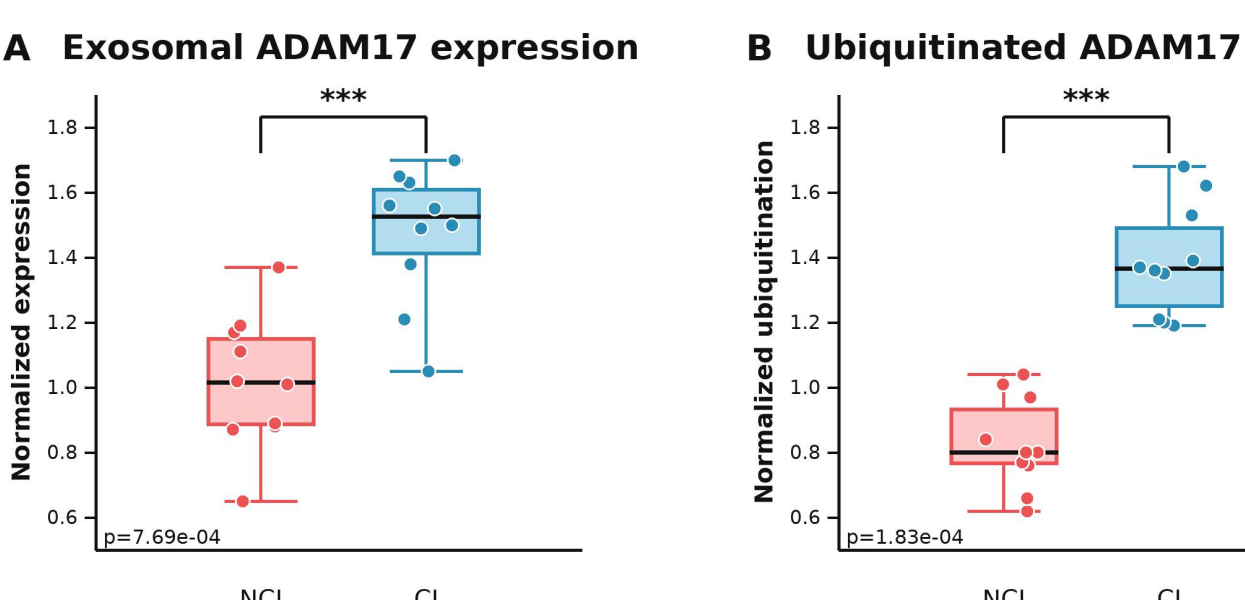
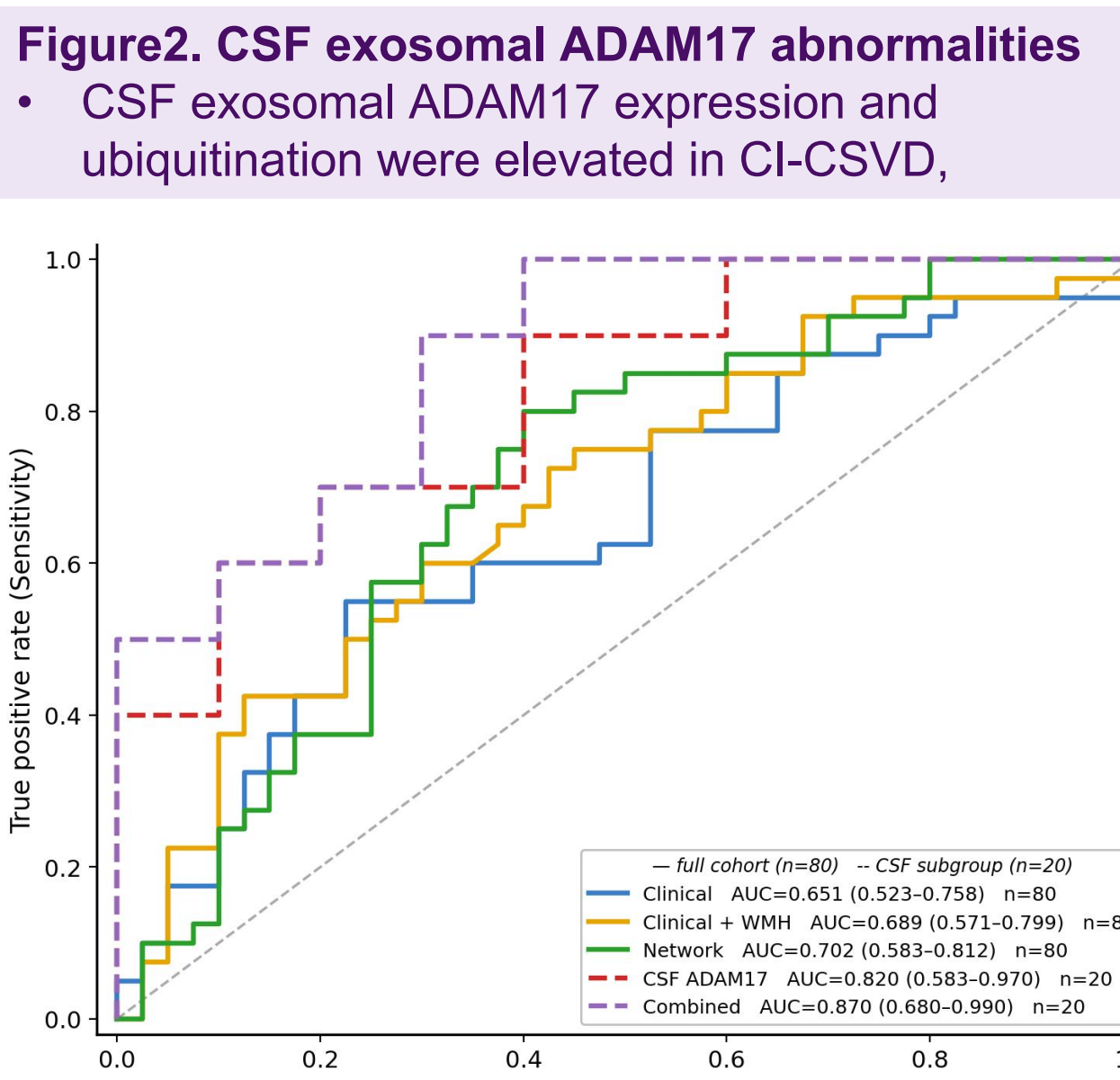


CSF Exosomal ADAM17 and Functional Network Segregation in Cognitive Heterogeneity of Cerebral Small Vessel Disease

#11881

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Key Takeaway: CSF exosomal ADAM17 and frontoparietal network disruption may help explain cognitive heterogeneity in CSVD beyond WMH burden and show exploratory value for risk stratification.

BACKGROUND	METHODS	RESULTS	CONCLUSIONS								
WMH is the core MRI marker of CSVD, but lesion burden alone cannot explain cognitive heterogeneity. We investigated whether CSF exosomal ADAM17, a potential marker of neuroinflammatory sheddase activation, and functional network segregation, especially within the frontoparietal control network, are associated with CSVD-related cognitive impairment.	<table><tr><td>Participants</td><td>80 CSVD patients (40 CI, 40 CN); 20 with CSF (10/group)</td></tr><tr><td>MRI</td><td>rs-fMRI → SyS based on Yeo 7-network parcellation; Fazekas WMH grading;</td></tr><tr><td>CSF</td><td>Ultracentrifugation → exosomes; ADAM17 (WB); ubiquitination (IP-WB); proteolytic activity (fluorogenic);</td></tr><tr><td>Analysis</td><td>Group comparison; multivariable regression adjusted for age, sex, education, and Fazekas score; Pearson correlation.</td></tr></table>	Participants	80 CSVD patients (40 CI, 40 CN); 20 with CSF (10/group)	MRI	rs-fMRI → SyS based on Yeo 7-network parcellation; Fazekas WMH grading;	CSF	Ultracentrifugation → exosomes; ADAM17 (WB); ubiquitination (IP-WB); proteolytic activity (fluorogenic);	Analysis	Group comparison; multivariable regression adjusted for age, sex, education, and Fazekas score; Pearson correlation.	Figure 1. Functional network disruption in CI-CSVD  • Functional network segregation was altered in CI-CSVD, with the most consistent cognitive association observed in the frontoparietal control network. Figure 2. CSF exosomal ADAM17 abnormalities  • CSF exosomal ADAM17 expression and ubiquitination were elevated in CI-CSVD, Figure 3. Exploratory discriminative performance  • Adding network and CSF exosomal markers improved discrimination beyond clinical and WMH models, with the combined model showing the highest AUC.	CSF exosomal ADAM17 may capture neuroinflammation-related synaptic vulnerability, while frontoparietal control network disruption may provide a network-level explanation for cognitive heterogeneity in CSVD beyond WMH burden. These markers may also offer exploratory value for cognitive risk stratification.
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CSF exosomal ADAM17 may capture neuroinflammation-related synaptic vulnerability, while frontoparietal control network disruption may provide a network-level explanation for cognitive heterogeneity in CSVD beyond WMH burden. These markers may also offer exploratory value for cognitive risk stratification.